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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/294,539	04/19/1999	CHERN MAW SHENQ	23070-948	6246

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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 09/22/2004

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/294,539	MAW SHENQ ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004 and 23 May 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,13,22,30-32,43,52,60,62 and 70-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,30-32,52,60 and 70-79* is/are rejected.

7)☒ Claim(s) *13,22,43,52 and 62* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-2, 13, 22, 30-32, 43, 52, 60, 62 and 70-79 are pending.

2. The indication of allowance given in the interview summaries mailed 8 December 2002 and 22 May 2002 is withdrawn.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The rejections of claims 1, 4, 30-31, 34 and 60 are rejected under 35 U.S.C. 102(e) as being anticipated by each of Uknes et al (US Patent 5,986,082, filed December, 1996) and Ryals et al (US Patent 6,031,153, filed December, 1996) is withdrawn in light of Applicant's amendment of the claims.

5. The rejection of claims 1, 4, 30-31, 34 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Ausubel et al (WO98/06748) is withdrawn in light of Applicant's amendment of the claims.

6. The rejection of claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Cao et al (1997, Cell 88:57-63) is withdrawn in light of Applicant's amendment of the claims.

7. The rejection of claims 1-2, 4, 13, 22, 30-32, 34, 43, 52, 60 and 62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in light of the Declaration of Pamela Ronald, filed 10 January 2001.

8. The rejection of claims 1-2, 4, 13, 22, 30-32, 34, 43, 52, 60 and 62 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter that Applicant regards as the invention is withdrawn in light of Applicant's amendment of the claims.

Claim Rejections - 35 USC § 112

9. Claims 1-2, 30-32, 60 and 70-79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids that encode SEQ ID NO:4, plants transformed with the nucleic acid and a method of using it to enhance pathogen resistance, does not reasonably provide enablement for all nucleic acids encoding a protein that is 80% identical to SEQ ID NO:4, plants transformed with the nucleic acid and a method of using it to enhance pathogen resistance,. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is modified from the rejection set forth in the Office action mailed 9 August 2001, as applied to claims 1-2, 4, 30-32, 34 and 60. Applicant's arguments filed 9 January 2002 have been fully considered but they are not persuasive.

The claims are broadly drawn to nucleic acids encoding a protein that is 80% identical to SEQ ID NO:4, plants transformed with those nucleic acids, and methods of using those nucleic acids to enhance resistance to pathogens in a plant.

The specification (pgs 28-30) teaches the isolation of rice genes that encode protein that can interact with *Arabidopsis* NPR1 in a yeast two-hybrid system. Two of these rice genes (MN1 and PN1) were used in another yeast two-hybrid assay to isolate additional rice genes that

encode proteins that interact with proteins encoded by the first set of rice genes. SEQ ID NO:3 (NH1) encodes one of these latter proteins.

The instant specification, however, fails to provide guidance for which amino acids of the protein encoded by SEQ ID NO:3 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain the activity of SEQ ID NO:4. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional protein.

It cannot be predicted by one of skill in the art that nucleic acids encoding a protein that is 80% identical to SEQ ID NO:4 encode proteins with the same function as that of SEQ ID NO:4. The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252), who teach that a replacement of aspartic acid at position 47 with alanine or asparagine in transforming growth factor alpha had no effect, but that replacement with serine or glutamic acid sharply reduced biological activity (see the abstract). Small changes in amino acid sequence can completely modify enzymatic function; Broun et al (1998, Science 282:1315-1317) teach that a change of four amino acids converts an oleate 12-desaturase to a hydroxylase. Thus, Lazar et al and Broun et al demonstrated that one or few amino acid substitutions could dramatically affect the biological activity and the structure-function characteristics of a protein.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (*supra*) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions

with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, are encoded by nucleic acids that have much more than 50% identity to the original nucleic acid.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate a multitude of nucleic acids encoding a protein that is 80% identical to SEQ ID NO:4, plants transformed with those nucleic acids, and methods of using those nucleic acids to enhance resistance to pathogens in a plant.

Applicant did not address this enablement rejection.

10. Claims 1-2, 30-32, 60 and 70-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 9 August 2001, as applied to claims 1-2, 4, 13, 22, 30-32, 34, 43, 52, 60 and 62. Applicant's arguments filed 9 January 2002 have been fully considered but they are not persuasive.

The claims are broadly drawn to a multitude of nucleic acids encoding a protein that is 80% identical to SEQ ID NO:4. In contrast, the specification only describes a coding sequence

from rice that comprises SEQ ID NO:3. Applicant does not describe other nucleic acids encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described nucleic acids that encode a protein that is 80% identical to SEQ ID NO:4 within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997) at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.
> ... A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.
> ... the claimed genera of vertebrate and mammal cDNA are not described by the general language of the '525 patent's written description supported only by the specific nucleotide sequence of rat insulin.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

Applicant did not address this enablement rejection.

11. Claims 1-2, 13, 22, 30-32, 43, 52, 60, 62 and 70-79 are free of the prior art given the failure of the prior art to teach or suggest an isolated nucleic acid encoding a protein with 80% identity to SEQ ID NO:4.

12. Claims 13, 22, 43, 52 and 62 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne R. Kubelik, Ph.D.
September 17, 2004

ANNE KUBELIK
PATENT EXAMINER